Immunoterapia. Quadri clinici e gestione delle tossicità.

CRITICITÀ

Verona, 9 Aprile 2016
Daniela Iacono
UOC Oncologia Medica
Azienda Ospedaliera Sant'Andrea – Roma

Immunotherapy : the new era in (N)SCLC treatment

The use of immune checkpoint inhibitors represents one of the most exciting breakthroughs in the history of lung cancer therapy:

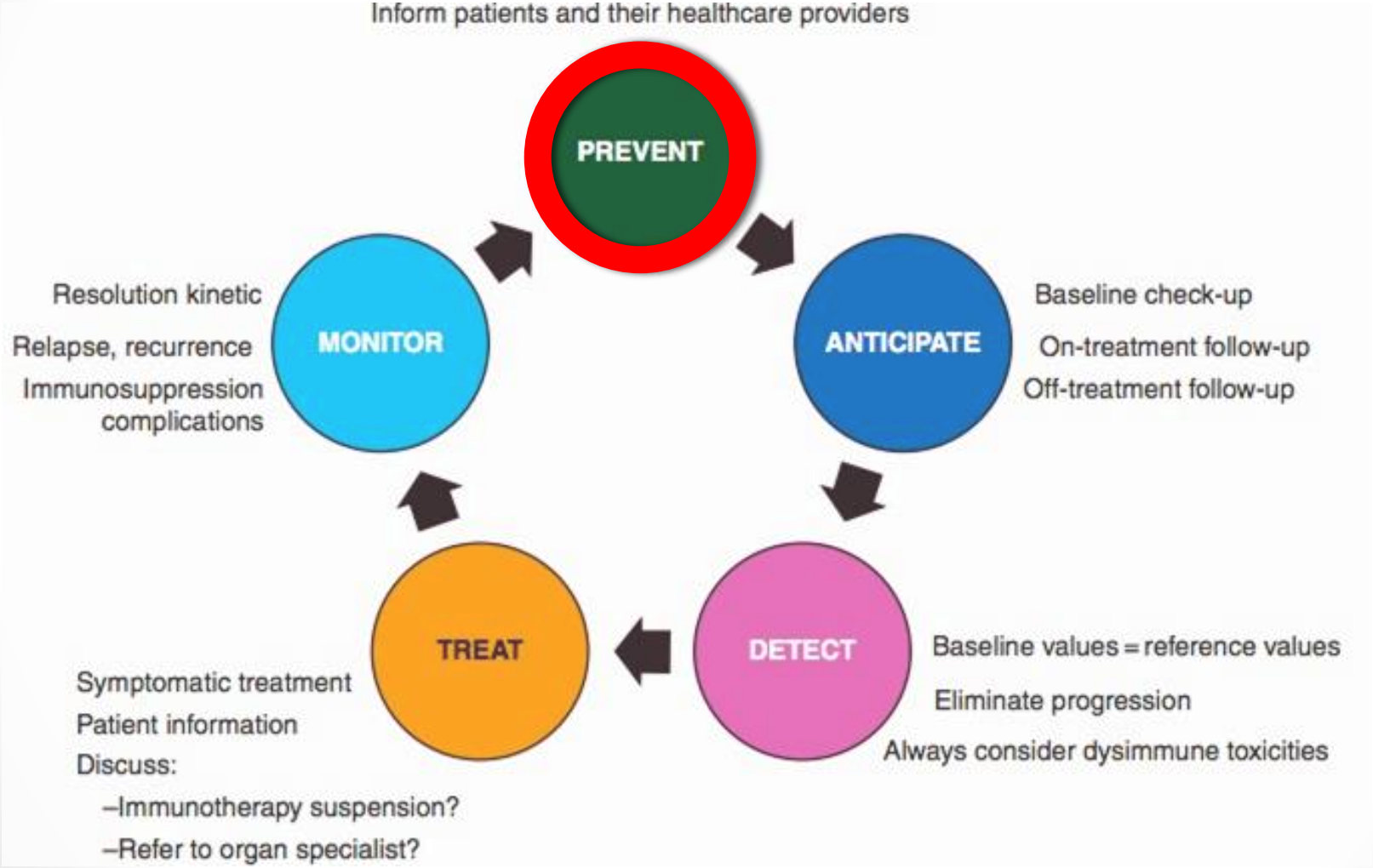
- Significant improvement in OS
- Significant improvement in PFS
- Long lasting responses
- Significant tumor shrinkage → symptoms relief

Immunotherapy : the new era in (N)SCLC treatment

The use of immune checkpoint inhibitors implicates a new toxicity profile

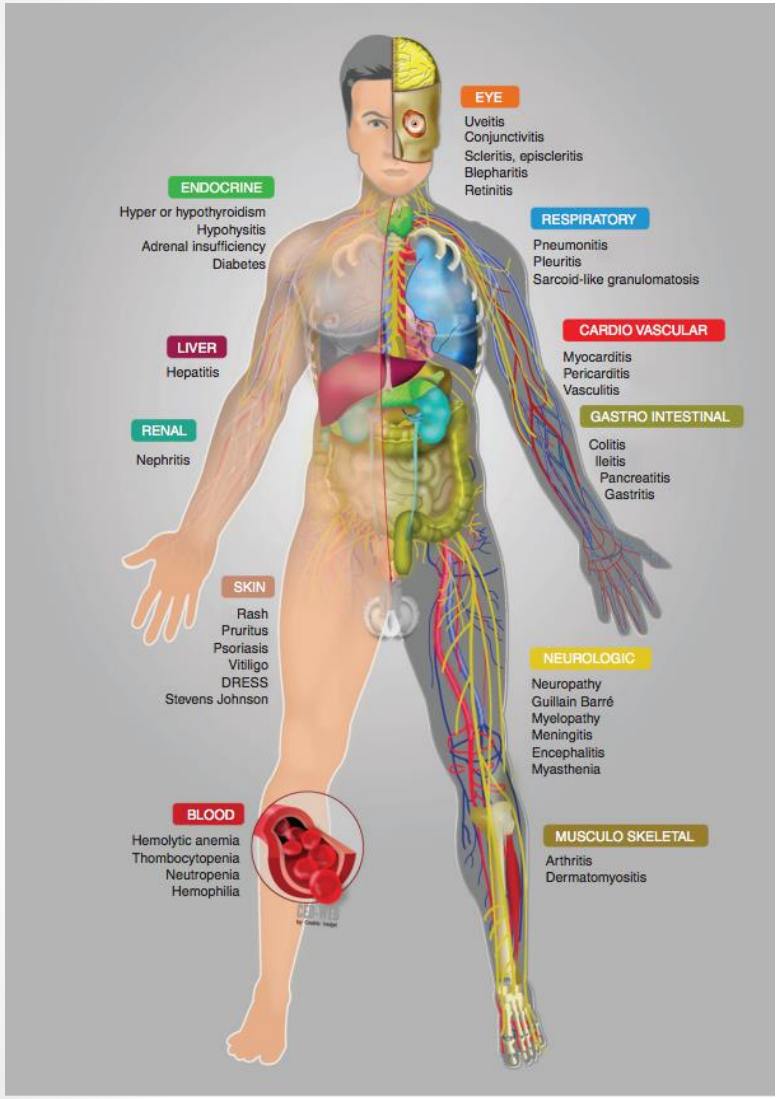
- Different mechanisms of adverse events' development (IrAEs)
- New protocols for the management of the toxicity
- Requirement of multidisciplinary team for the management of IrAEs

The five pillars of immunotherapy toxicity management



Champiat S. et al. Ann of Oncol 16, 2016

Prevent (1): knowledge of the drug



Before prescribing immune-checkpoints to their patients, oncologists need to be aware of their **spectrum of toxicity**:

- Eye
- Endocrine
- Respiratory
- Cardio Vascular
- Liver
- Renal
- Skin
- Neurologic
- Musculo-Skeletal
- Blood

Champiat S. et al. Ann of Oncol 16, 2016

Prevent (2): knowledge of the patient

- Personal and family history of autoimmune diseases
- Tumoral infiltration
  - Pulmonary lymphangitis
  - Caricinomatous meningitis
- History of chronic infection (HBV, HCV, HIV)
- Co-medications

Prevent (3): inform patients and their care givers

- Pts and their caregivers should be informed of their specific risk of immune-related toxicity development
- Occurrence of new symptoms or worsening of preexistent symptoms should be rapidly reported to the physician
- Pts must be informed tha IrAEs may occur at any time: at the beginning, during or after treatment discontinuation

Prevent (4): knowledge of the frequency and timeline occurrence of IrAEs

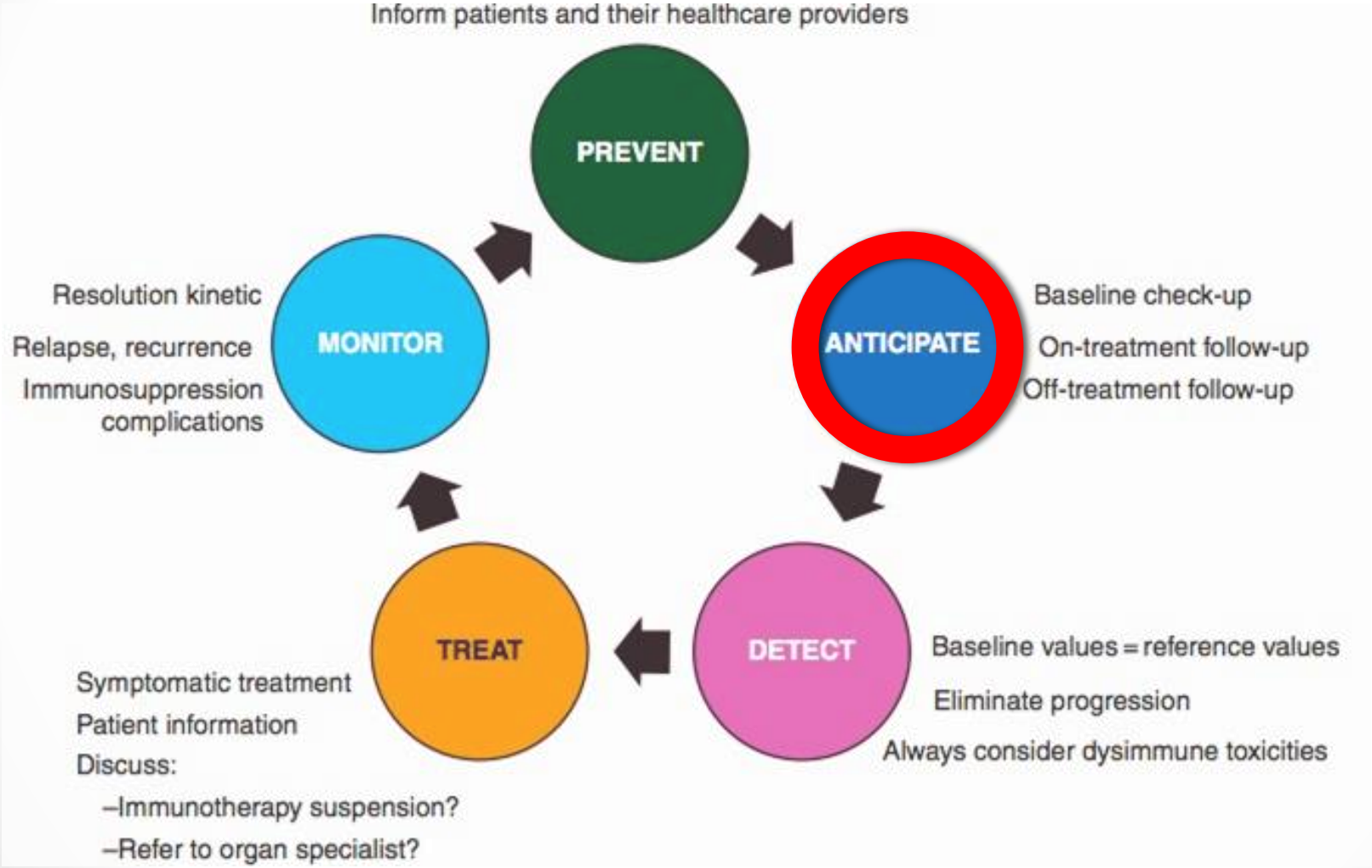
- IrAEs are **frequent**:
  - 90% of patients treated with CTLA4 antibody
  - 70% of patients treated with PD1/PDL1 inhibitors

But

- In most of the cases IrAEs are low or mild grade of severity
- Most of IrEAs are steroid-sensitive
- Most of IrEAs resolve within 6-12 weeks

- **Algorithms for the management of IrAEs are available!**

The five pillars of immunotherapy toxicity management

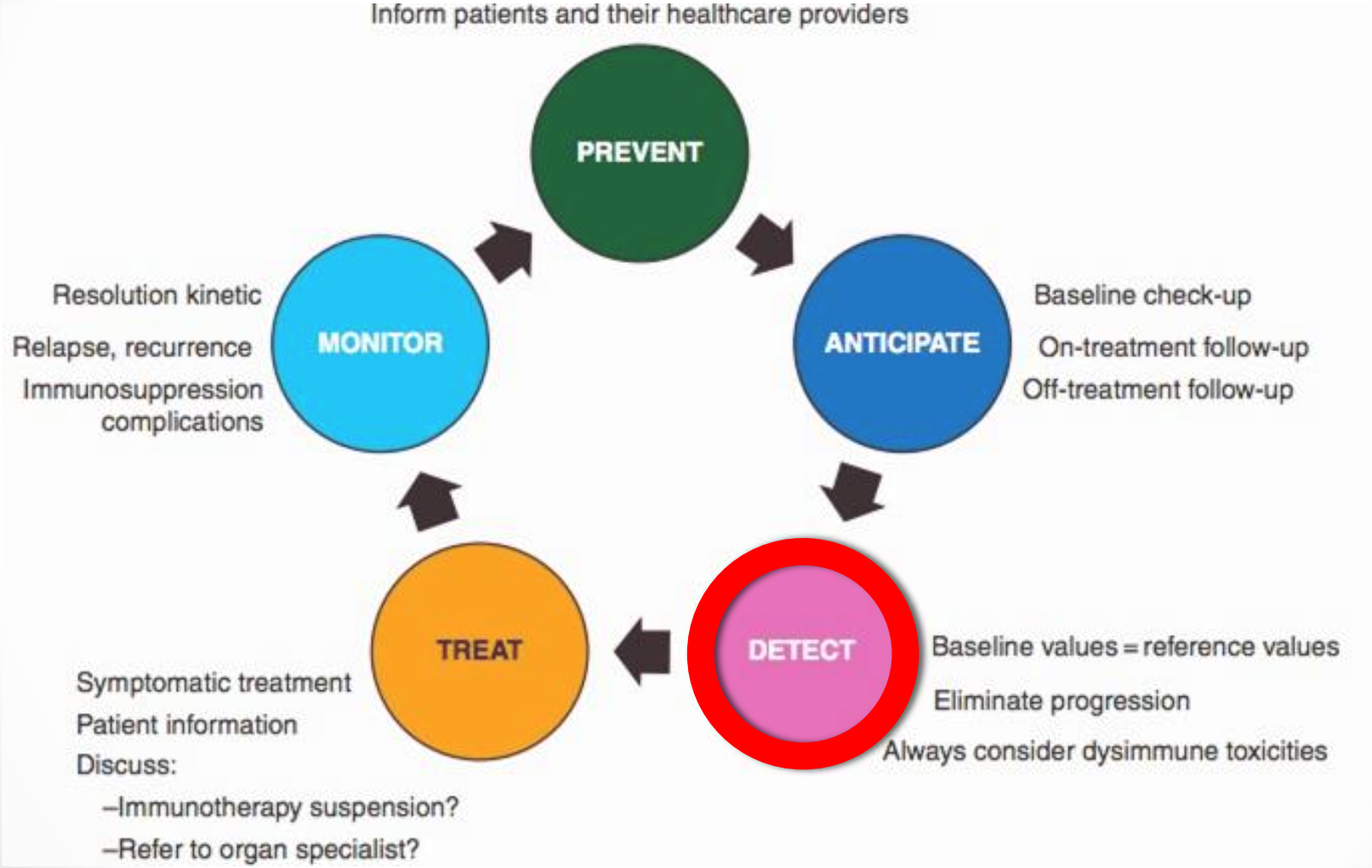


Champiat S. et al. Ann of Oncol 16, 2016

Anticipate

- Report of toxicity sequelae from previous treatment
- Physical examination
- Baseline laboratory tests and imaging for comparison with same type of evaluation during the treatment
- Clinical and biological follow-up after treatment discontinuation

The five pillars of immunotherapy toxicity management



Champiat S. et al. Ann of Oncol 16, 2016

Detect (1)

- Three potential etiologies for new symptoms occurrence or symptoms worsening during immunotherapy:
  1. Disease progression
  2. Fortuitous event
  3. Treatment-related dysimmune toxicity

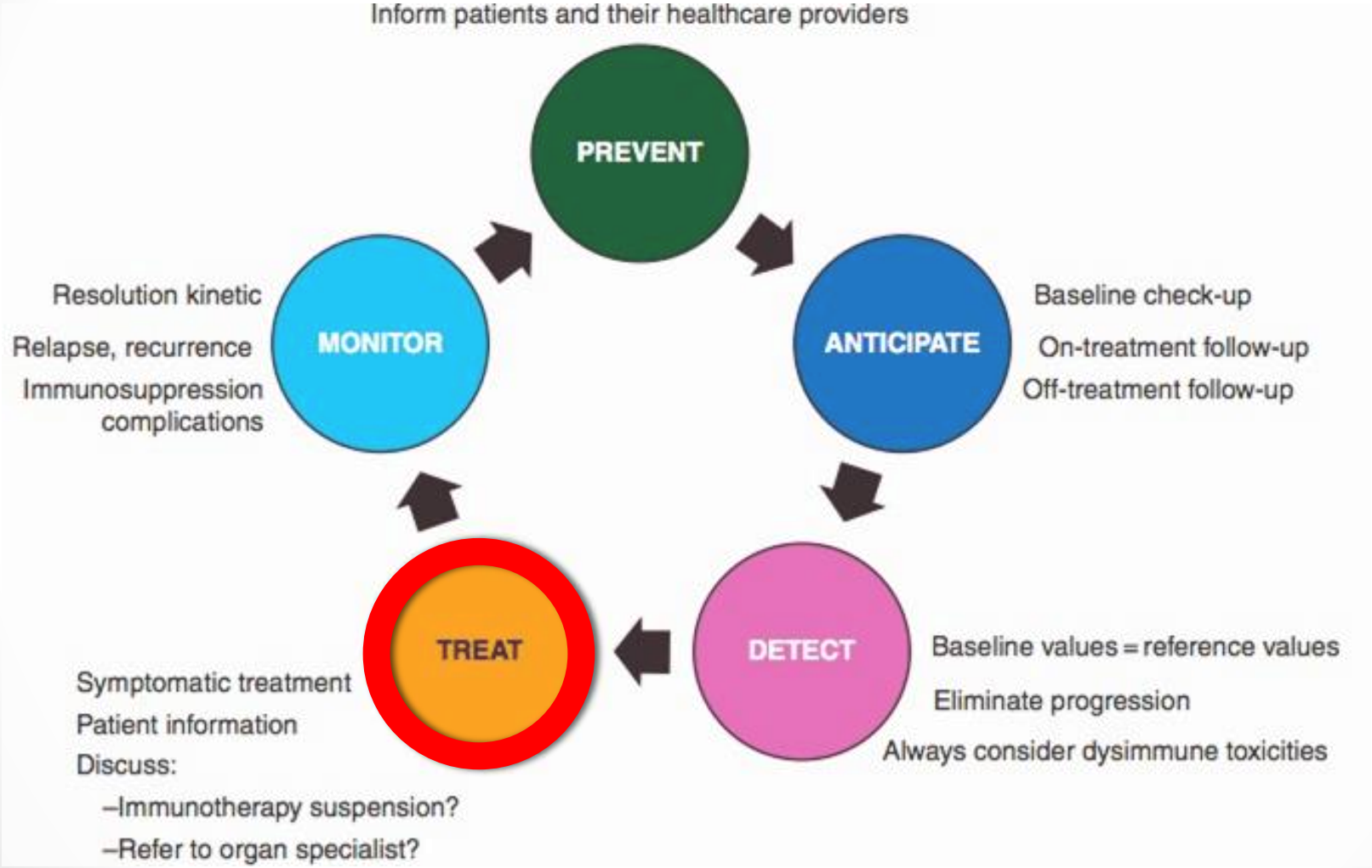
Keep in mind:

- The most frequent adverse events are related to disease progression
- Neglecting immune-related toxicities could be potentially fatal

Detect (2)

- Any new symptom or laboratory abnormality should be attentively monitored and appropriately explored
- Each IrAE has its own management protocol
- DO NOT manage an IrAEs in the same way of a chemotherapy toxicity

The five pillars of immunotherapy toxicity management

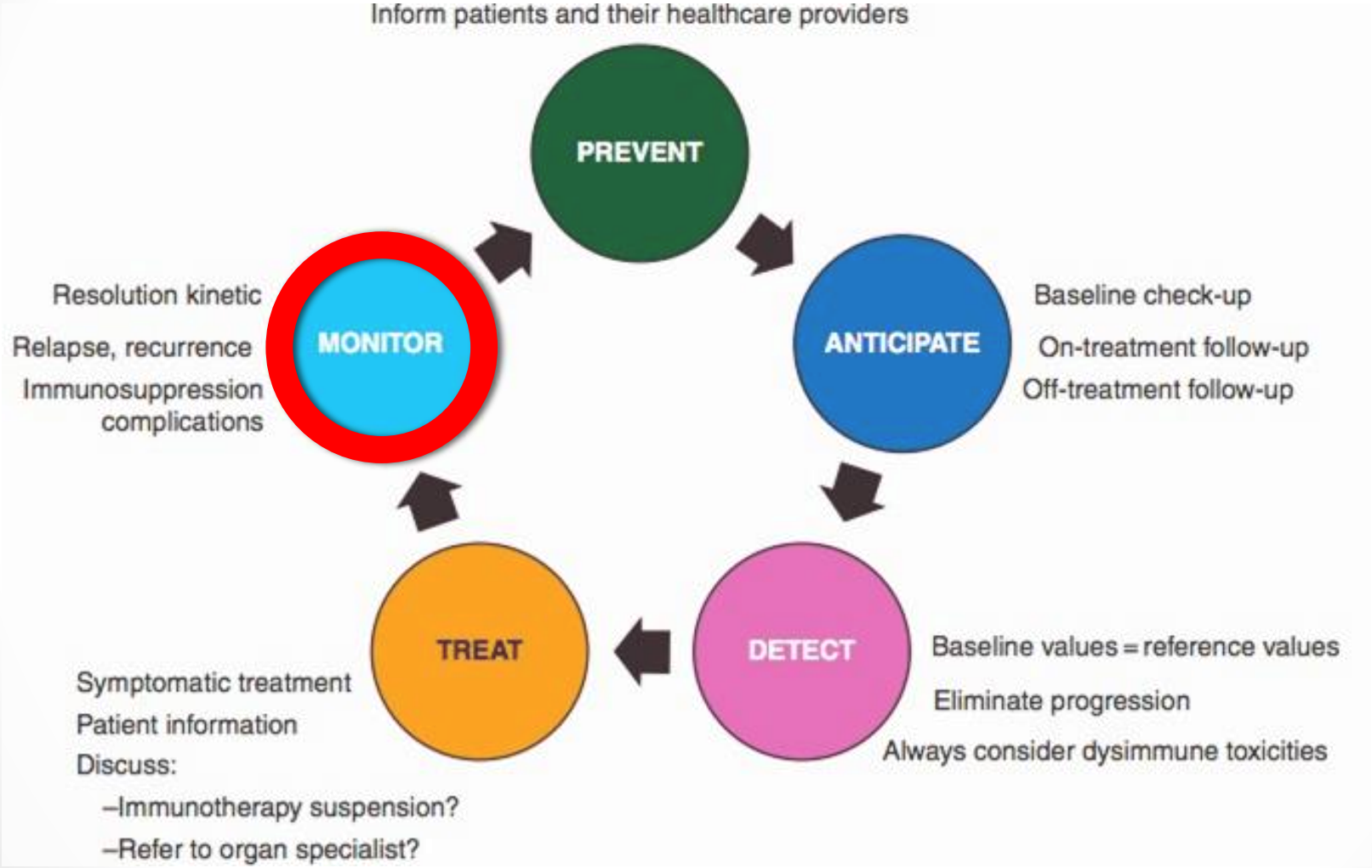


Champiat S. et al. Ann of Oncol 16, 2016

Treat (1)

- Close monitoring
- Toxicity grading
- Ambulatory versus inpatient care
- Corticotherapy
- Other immunosoppressive drugs
- Immunotherapy suspension or termination
- Patient information and how to self-monitor clinical elements

The five pillars of immunotherapy toxicity management



Champiat S. et al. Ann of Oncol 16, 2016

Monitor (1)

- The time needed for IrAE resolution can highly vary across the various types of toxicities

- Preliminary data seem to show that systemic immunosuppressants used for IrAEs might not have such a negative impact on efficacy

Downey, S. G. et al. Clin. Cancer Res. 13 (22 Pt 1) 6681–6688 (2007).

The End

Daniela Iacono
dani.iacono@gmail.com